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Research in space: in search of meaning

Life science research aboard the International Space Station has come under scrutiny for its costs and apparent lack of returns

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Ground Control to Major Tom
Ground Control to Major Tom
Take your protein pills and put your helmet on
Ground Control to Major Tom (Ten, Nine, Eight, Seven, Six)
Commencing countdown, engines on (Five, Four, Three)
Check ignition and may God's love be with you (Two, One, Liftoff)—David Bowie: Space Oddity

Humans have been going into space for a number of reasons: to "beat the other side" during the Cold War, out of curiosity, to make the first tentative steps into the great beyond or simply "because it's there". Yet, to justify continued or even a permanent presence of humans in space now requires better arguments: the aggressive space programmes by China and India, for instance, serve to demonstrate their advanced financial, technological and organizational capacity and international prestige. Private companies are now exploring ways to get humans off the planet for commercial reasons and the military has always had a long-standing interest in heaving material and humans into orbit.

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When the first components of the International Space Station (ISS) were launched into orbit in 1998, scientific research was put forward as a major argument for establishing a permanent presence of humans in space; the ISS was soon expanded with several laboratory modules to conduct a wide range of experiments in microgravity (Fig 1). However, at a time of prolonged financial and political crisis, the future of science in space is uncertain. Intangibles such as "inspirational value" and "motivation for educational excellence" are no longer sufficient to spur significant investments if the results from the ISS laboratories are neither scientifically relevant nor applicable to use on Earth. The US administration has recently proposed to extend ISS operations until 2024, but given the current strained relations with Russia—which plays a vital role in transporting astronauts and materials to and from the ISS through its Soyuz capsules—even access is getting precarious. In the light of these and other problems, research in space needs to refocus its aims and rethink its role.

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As of March 2015, ISS has enabled more than 2,700 researchers from 95 countries to conduct more than 1,900 experiments in microgravity, often carried out through international collaboration (http://www.nasa.gov/sites/default/files/atoms/files/iss_utilization_statistics_0-42_final_mcbapproved.pdf). Research activity ranges from astronomy to fundamental physics and materials science to medicine and biology. Biologists have used the ISS laboratory modules to study the human body's response to extended periods in microgravity, and also the development, life cycle and behaviour of micro-organisms, plants and animals and how they are influenced by space radiation, gravitational effects and so on. "In the areas of human health, innovative technology, education and observations of Earth from space, there are already demonstrated benefits to people back on Earth", wrote NASA's chief scientist for the ISS programme Julie Robinson and colleagues [1]. "Lives have been saved, station-generated images assist with disaster relief, new materials improve products, and education programmes inspire future scientists, engineers and space explorers".

> *"The overall problem for biomedical research in space, however, is the apparent lack of a comprehensive strategy to maximize the benefits in light of the substantial costs . . ."*

Space medicine has been the most relevant research field. Studying and understanding the impact of microgravity, radiation and prolonged isolation on human physiology and psychology (Fig 2) are an important prerequisite for longer trips into space such as a manned mission to Mars. The astronauts on the ISS are continuously monitored for various physical parameters and often lend themselves to experimentation. Bone loss is a particularly serious problem for astronauts

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Figure 1. International Space Station.
First launched in 1998, and continuously inhabited since November 2000, ISS is a joint project among five participating space agencies: NASA, ESA, Canadian Space Agency, Russian Federal Space Agency (Roscosmos) and Japan Aerospace eXploration Agency (JAXA). Credit: ESA.

who remain in a microgravity environment for longer periods of time [2]. Owing to the lack of normal weight-bearing activities, bone metabolism changes rapidly: calcium is released from bone, which suppresses parathyroid hormone; this in turn induces a drop in circulating 1,25-dihydroxyvitamin D and leads to a decrease in calcium absorption. Even with countermeasures such as extensive exercise, crew members currently return to Earth with an average bone mass loss of 1–2% for each month spent on the ISS. A number of studies showed that bone loss can be reduced with an effective exercise programme and the proper intake of calcium and vitamin D, plus anti-resorptive agents like bisphosphonates. The molecular mechanisms behind bone loss in space are also actively investigated, and several regulatory pathways are being explored as targets for therapeutic interventions [2].

Other high-profile research activities on the ISS focus on micro-organisms as ubiquitous and natural constituents of any environment. When going into space, astronauts inevitably transport microbial communities with the air, water, food and within themselves. Scientists are therefore interested in how micro-organisms adapt to the microgravity environment, and how that might impact bacterial physiology, growth rate and antibiotic resistance or virulence, with obvious implications for manned space missions.

A different batch of studies investigates whether extremophilic organisms can survive in extraterrestrial environments. In parallel, these studies also provide basic information on the possibilities of resistance and protection of living organisms, including humans, from radiation damage. “Until a few years ago, it was largely believed that no terrestrial organism is able to survive under conditions found in space, which cannot be adequately simulated on Earth”, said botanist and astrobiologist Silvano Onofri at Tuscia University in Viterbo, Italy. “Now, some organisms have been shown to withstand the conditions of space, enabling the possibility of a transfer of life from planet to planet”.

Colonies of microscopic fungi of the genus *Cryomyces*, which normally inhabit Antarctic rocks, were exposed to radiation and high vacuum conditions aboard the ISS for 18 months as part of the ESA’s EXPOSE-E mission [3,4]. Isolated from the McMurdo Dry Valleys of Antarctica, one of the most hostile environments on Earth, these organisms live on the edge between life and death, with water available for only a few days a year and severe temperatures. Since their natural environment is considered the closest terrestrial analogue for Mars, researchers have speculated that if life has

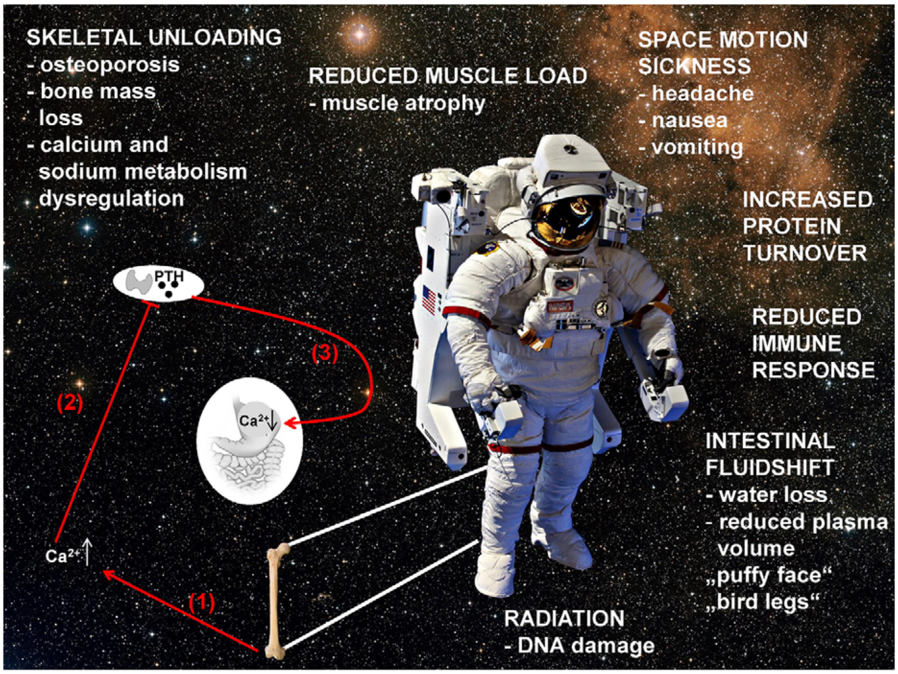

Figure 2. The most important physical health problems of humans in space.
Examples of the most critical health concerns for space travellers, including reduced tissue load, radiation, space motion sickness, increased protein turnover, reduced immune response, disruption of vision and taste, cardiovascular problems, orthostatic intolerance, disturbance of the biological clock and intestinal fluid shifts. In astronauts, bone loss in response to microgravity causes the release of calcium from bone (1), which suppresses parathyroid hormone (2). This suppression of parathyroid hormone is in turn associated with a drop in circulating 1,25-dihydroxyvitamin D and a decrease in calcium absorption (3). Reproduced from [2], with permission.

ever existed on the Red Planet, it might have shared similarities with Antarctic *cryptoendolithic* fungi. The studies aboard the ISS found that more than 60% of the fungal cells had remained intact after exposure to Mars-like conditions, and some 10% of the samples were able to proliferate and form colonies when brought back to Earth [3,4]. “The experiments on the ISS, in outer space environment, but with radiation and simulated Martian atmosphere, give us some clues on the chances of survival under such conditions, and on the traces that organisms could have left in extraterrestrial rocks”, Onofri commented.

Another line of research aboard the ISS tries to understand how flowering plants grow in microgravity (Fig 3). The results may become essential for long-distance space flights and for establishing self-sustaining extraterrestrial human colonies to provide fresh food sources for crew members. Researchers claim that the systems developed might also have implications for improving plant growth and biomass production on Earth, for example in helping in the creation of more productive greenhouses. NASA installed its “Veggie”—a vegetable production facility able of growing salad-type crops and other higher plants (https://www.nasa.gov/content/veggie-plant-growth-system-activated-on-international-space-station)—on the orbiting laboratory in early May of 2014, and the first crop, red romaine lettuce, was successfully grown and even consumed by crew members. The next experiment was a batch of zinnia flowers (Fig 3), a more difficult plant to grow and thus considered a good precursor for more important crops, such as tomatoes.

Protein crystallization is one of the fields that are often cited for the necessity of moving research into space, where sedimentation and convection flow do not obstruct the crystallization process, which would allow for the production of crystals of larger size and higher quality than those obtainable on Earth (Fig 4) [5]. The better and larger the crystals, the better X-ray diffraction analysis can determine the 3D structure of a protein to understand its biological role and mechanism of action. This, the argument goes, could then improve rational drug design for new therapies. An example is haematopoietic prostaglandin D synthase (HPGDS), a protein expressed in muscle fibres of patients with Duchenne muscular dystrophy. A team at the Osaka Bioscience Institute in Japan determined the 3D structure of HPGDS in complex with specific inhibitors; most of the space-grown crystals yielded better X-ray diffraction patterns than the terrestrially grown ones [6].

Overall, however, microgravity crystallization has not spurred widespread enthusiasm, and many believe its impact on the field of structural biology has been limited (http://www.nap.edu/read/9785/chapter/1#xi). “Now, the ability to use exceptionally small amounts of material on Earth using high-precision, ultra-powerful X-ray sources has allowed materials developed for ground-based crystallography that exceed what is obtained from research using space-based materials”, wrote astrobiologist and former NASA employee Keith Cowing (http://nasawatch.com/archives/2015/09/nasa-and-casis-1.html). He added that crystallography itself is being eclipsed by new methods, such as cryo-electron microscopy, that offer valuable structural information without the trouble and costs of performing experiments in space.

“Since the money that funds cosmic endeavours comes from taxpayers, the quest for diversity and public attention is understandable but does not necessarily guarantee scientific excellence”

Not everyone agrees. “I continue to be convinced, largely by previous successes in space, that microgravity has a substantial role to play in macromolecular crystal growth research”, said structural biologist Alexander McPherson, from the University of California, Irvine. “This seems to me to be particularly true with regard to large, biologically important structures such as viruses and protein–nucleic acid complexes where transport phenomena play a significant part”. What is needed though is a long-term commitment to pursue the scientific aspects of the process, namely the physics of

Figure 3. Fresh food grown in space.
(A) NASA plans to grow food on future spacecraft and on other planets as a food supplement for astronauts. Fresh foods, such as vegetables, provide essential vitamins and nutrients that will help enable sustainable deep space pioneering. (B) *Zinnia* flowers are starting to grow in the International Space Station's Veggie facility as part of the VEG-01 investigation. Veggie provides lighting and nutrient supply for plants in the form of a low-cost growth chamber and planting "pillows" to provide nutrients for the root system. These plants appear larger than their ground-based counterparts and scientists expect buds to form on the larger plants soon. The Veggie facility supports a variety of plant species that can be cultivated for educational outreach, fresh food and even recreation for crew members on long-duration missions. The facility has also grown lettuce, which was then consumed by the crew. Understanding how flowering plants grow in microgravity can be applied to growing other edible flowering plants, such as tomatoes. Credit: NASA.

crystallization as it occurs in the absence of gravity, McPherson added.

The overall problem for biomedical research in space, however, is the apparent lack of a comprehensive strategy to maximize the benefits in the light of the substantial costs to transport material and humans into orbit. Research that does require a human presence in space, such understanding the mechanisms of the human physiological alterations that occur in microgravity, is not particularly privileged with respect to other, less compelling topics. When selecting the experiments for the ISS laboratories, there seems to be greater attention to media and public appeal (there is a "Student Spaceflight Experiments Programme") or to potential and unspecified "benefit to Earth" rather than scientific pay-off or a real necessity of performing such experiments in orbit.

Since the money that funds cosmic endeavours comes from taxpayers, the quest for diversity and public attention is understandable but does not necessarily guarantee scientific excellence. The feeling that research performed on the orbiting laboratory has been rather poor, and not in line with the expectations of the scientific community, has risen to an alarming level (http://www.space.com/9435-international-space-station-worth-100-billion.html). In a 2011 report, the US National Research Council remarked that NASA was "poorly positioned to take full advantage of the scientific opportunities offered by the now fully equipped and staffed ISS laboratory, or to effectively pursue the scientific research needed to support the development of advanced human exploration capabilities", although attributing this failure to "budgetary challenges and changing directions within the agency" [7].

In 2015 alone, NASA dedicated about US$3 billion, or one-sixth of its total $18 billion annual budget, to the ISS. In a recent post, mathematician and blogger Robert Walker claimed that, with its total cost of US$ 150 billion, ISS could well be the "most expensive single human artefact ever" (http://www.science20.com/robert_inventor/is_the_international_space_station_the_most_expensive_single_item_ever_built-156922). "I don't think those costs can be justified by the research alone, because we could have built it as a telerobotic facility operated from the ground, and done nearly all the same research for far less cost except the research into human effects of weightlessness", Walker wrote. "I don't know of any comparison study, but without the need to send humans there every few months, wouldn't be surprised if that would have cost an order of magnitude less".

This view is shared by other, more authoritative figures. "It's certainly not worth doing for any practical purpose, because the case for sending people into space is getting weaker with advances in automation and robotics, and

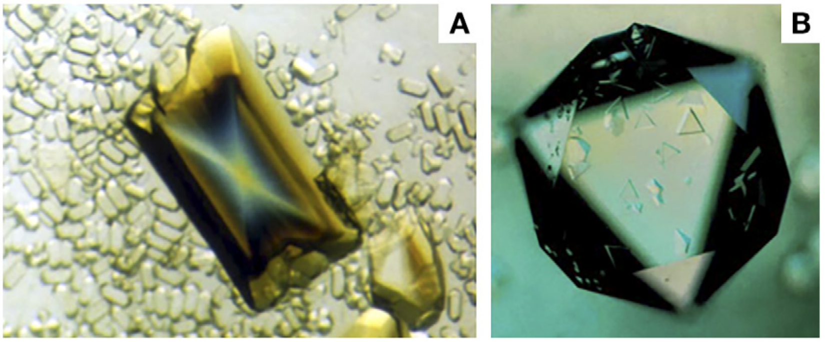

Figure 4. Protein crystals in space.
(A) A space-grown orthorhombic crystal of satellite tobacco mosaic virus (STMV) that is more than 1.5 mm in length and was about 30 times the volume of any STMV crystal ever grown on Earth. The small STMV crystals in the background formed after return to Earth when the retrograde solubility of the virus remaining in the mother liquor was induced to crystallize by the heat of the microscope lights used for observation. (B) An equivalent-sized cubic crystal of the same virus again far exceeding in dimensions any grown in an Earth laboratory. Reproduced from [5].

the future of all practical travel in space will be by robots", Lord Rees of Ludlow, former president of the Royal Society and renowned astronomer, told *The Times* (http://www.thetimes.co.uk/tto/science/article4444221.ece).

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"The high costs of the ISS are leading the international scientific community to envisage the use of other means, such as nanosatellites. At least, this is going on in the astrobiology field. These tools do not consent recovery of samples and then will give a tremendous boost to the automation of the analytical procedures", Onofri said. "However, for the time being, ISS provides an extraordinary facility for a range of research activities, including measuring the extent of human adaptation to the space conditions".

Research in space thus needs to evolve to focus more on what science needs. For the present, however, research on the ISS continues with the usual mix of studies that will "prepare astronauts for long-duration missions farther into the solar system" and "provide lasting benefits to life on Earth" (http://www.nasa.gov/mission_pages/station/research/news/destination_station_forum/). But research at the space station might be doomed anyway. "We're going to get out of ISS as quickly as we can", NASA's chief of human spaceflight William Gerstenmaier said recently, to concentrate on future challenges like returning to the Moon and getting ready to land on Mars (http://www.extremetech.com/extreme/219416-nasa-plans-to-leave-iss-to-focus-on-future-mars-mission). Even if ISS remains active until 2024, the deadline for users to build their experiments for the station could come 3 or 4 years earlier. And no one really knows what would be next. Rumours indicate that NASA and associated space agencies could either build a cheaper ISS to perform applied space research, or open the way to private firms (http://www.thespacereview.com/article/2785/1). It is not sure whether you can see the horizon of science clearer from space.

References

1. Robinson J (ed) (2015) *International Space Station Benefits for Humanity*, 2nd edn. Available at: http://www.nasa.gov/sites/default/files/atoms/files/jsc_benefits_for_humanity_tagged_6-30-15.pdf)
2. Grimm D, Grosse J, Wehland M, Mann V, Reseland JE, Sundaresan A, Corydon TJ (2016) The impact of microgravity on bone in humans. *Bone* 87: 44–56
3. Onofri S, de la Torre R, de Vera JP, Ott S, Zucconi L, Selbmann L, Scalzi G, Venkateswaran K, Rabbow E, Sánchez Inigo FJ *et al* (2012) Survival of rock-colonizing organisms after 1.5 years in outer space. *Astrobiology* 12: 508–516
4. Onofri S, de Vera JP, Zucconi L, Selbmann L, Scalzi G, Venkateswaran KJ, Rabbow E, de la Torre R, Horneck G (2015) Survival of antarctic cryptoendolithic fungi in simulated martian conditions on board the International Space Station. *Astrobiology* 15: 1052–1059
5. McPherson A, DeLucas LJ (2015) Microgravity protein crystallization. *Microgravity* 1: 15010
6. Tanaka H, Tsurumura T, Aritake K, Furubayashi N, Takahashi S, Yamanaka M, Hirota E, Sano S, Sato M, Kobayashi T *et al* (2011) Improvement in the quality of hematopoietic prostaglandin D synthase crystals in a microgravity environment. *J Synchrotron Radiat* 18: 88–91
7. National Research Council (2011) *Recapturing a Future for Space Exploration: Life and Physical Sciences Research for a New Era*. Washington, DC: National Academies Press. Available at: http://nap.edu/13048